BLUNDELL et al. Serial No. 09/820,745 December 22, 2004

IN THE CLAIMS:

Amend the claims as follows:

Claims 1-4. (Canceled)

- 5. (Currently Amended) A method for identifying an agent compound which modulates ketopantoate hydroxymethyltransferase (KPHMT) activity, comprising the steps of:
- (a) employing three-dimensional atomic coordinate data according to Table 1 to characterise at least one KPHMT binding <u>sitesites</u>;
 - (b) providing the structure of a candidate agent compound;
 - (c) fitting the candidate agent compound to the binding sites; and
 - (d) selecting the candidate agent compound.
 - 6. (Original) The method of claim 5 wherein:

a plurality of binding sites are characterised and a plurality of agent compounds are fitted to said sites; and

said agent compounds are linked to form a potential modulator compound.

- 7. (Original) The method of claim 5 wherein step (b) comprises selecting said candidate agent compound by computationally screening a database of compounds for interaction with said binding site.
 - 8. (Original) The method of claim 5 which comprises the further steps of:
 - (e) obtaining or synthesising the candidate agent compound; and
- (f) contacting the candidate agent compound with KPHMT to determine the ability of the candidate agent compound to interact with KPHMT.

Claims 9-10. (Canceled)

BLUNDELL et al. Serial No. **09/820,745** December 22, 2004

- 11. (Currently Amended) A method for determining the structure of a KPHMT homologue of the <u>ketopantoate hydroxymethyltransferase (KPHMT)</u> defined by Table 1, wherein said method comprises:
- (a) aligning a representation of an amino acid sequence of a KPHMT homologue of unknown structure with the amino acid sequence of KPHMT to match homologous regions of the amino acid sequences;
- (b) modelling the structure of the matched homologous regions of the KPHMT of unknown structure on the structure as defined by Table 1 of the corresponding regions of the KPHMT of Table 1; and
- (c) determining a conformation for the KPHMT of unknown structure which substantially preserves the structure of said matched homologous regions.

Claims 12-13. (Canceled)

14. (new) A computer-based method of rational drug design which comprises: providing the structure of the ketopantoate hydroxymethyltransferase (KPHMT) as defined by the coordinates of Table 1 or a root mean square deviation from the backbone atoms of less that 1.5 Å thereof;

providing the structure of a candidate agent compound; and

fitting the structure of the candidate to said structure of the KPHMT as defined by the coordinates of Table 1 or a root mean square deviation from the backbone atoms of less that 1.5 Å thereof.

15. (new) The method of claim 5 wherein said at least one KPHMT binding site is characterised by employing atomic coordinate data for at least two atoms from the

BLUNDELL et al. Serial No. 09/820,745 December 22, 2004

atoms of the residues Tyr25, Asp45, Ser46, Asp84, Lys112, Glu114, Tyr150, Lys151, Arg155, Glu181, Asp217, Lys228, Lys231, Phe229 and His261.

16. (new) The method of claim 5 wherein said atomic coordinate data includes data for KPHMT backbone atoms, the positions of said backbone atoms varying by less than a root mean square deviation of 1.5 Å from the corresponding positions of Table 1.